FIGURE 1

Expression Vector

Univector construct

cre mediated lox-recombination
select for Km + Ap resistance

FIGURE 2

A

pUNI 10
2220 bp

ori

Kan

lox

PolyA Site

TERM

HinD III(114)

Bgl II(1896)

PstI (1683)

BssHII(1335)

EcoRV(890)

XbaI(750)

NotI (401)
KpnI(409)
EcoRI(452)
XhoI(464)
NdeI(472)
NcoI(479)
BamHI(485)
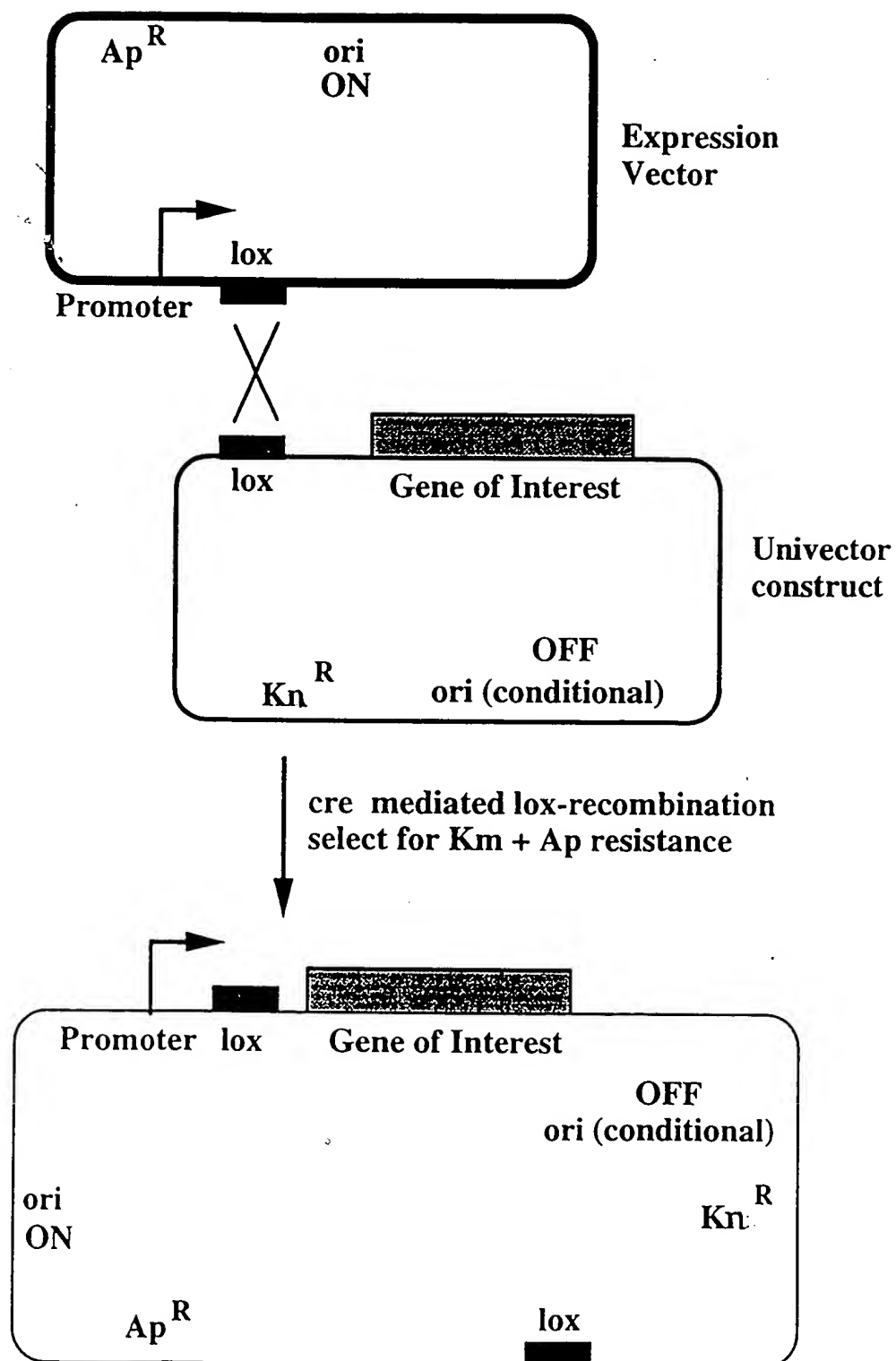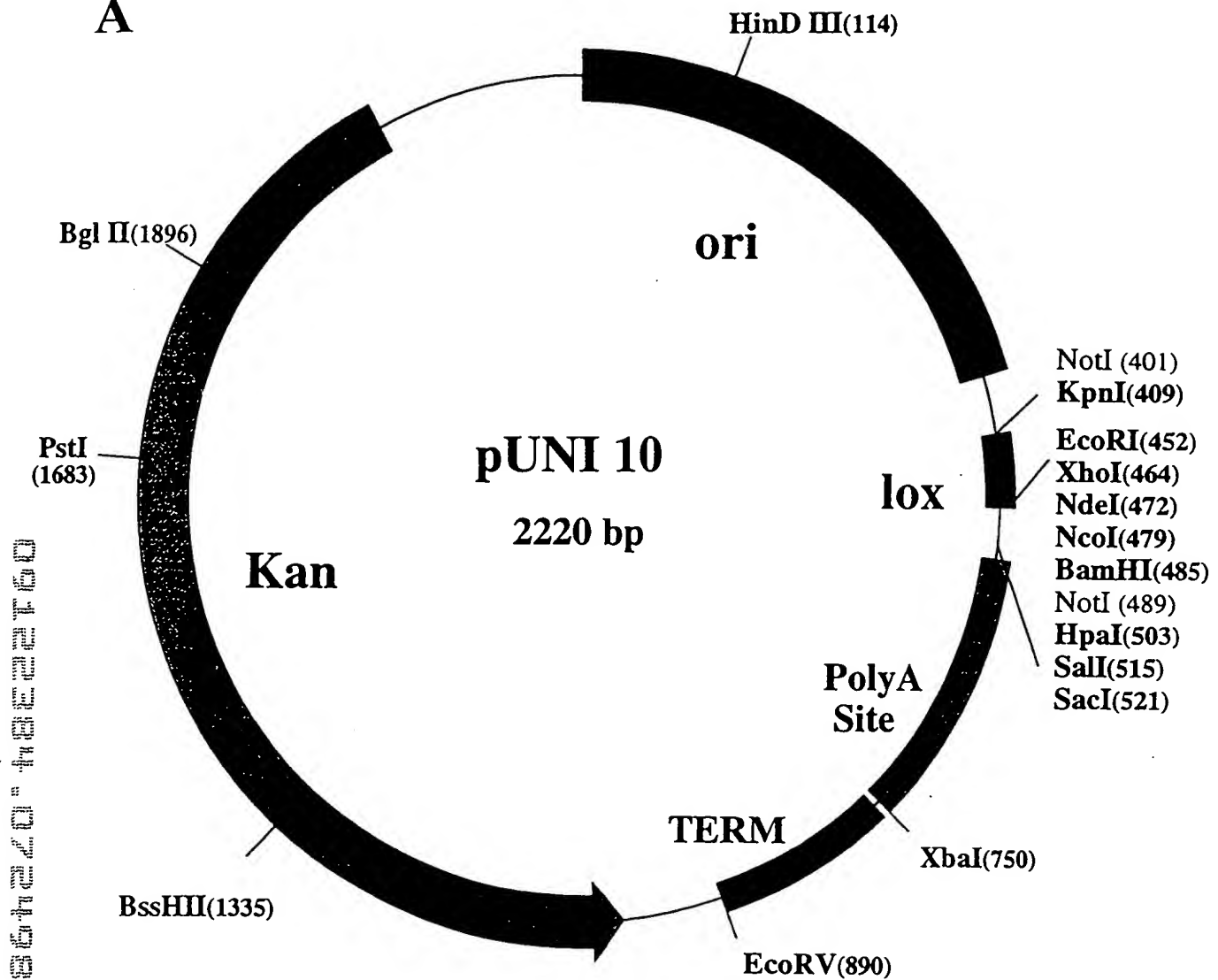NotI (489)
HpaI(503)
SalI(515)
SacI(521)

B

(401) NotI   KpnI   LOX
GC GGC CGC GGT ACC ATA ACT TCG TAT AGC ATA CAT TAT ACG AAG TTA TCT

EcoRI   SmaI   XhoI   NdeI   NcoI   BamHI   NotI
GGA ATT CCC CGG GCT CGA GAA CAT ATG GCC ATG GGG ATC CGC GGC CGC

HpaI   SalI   SacI
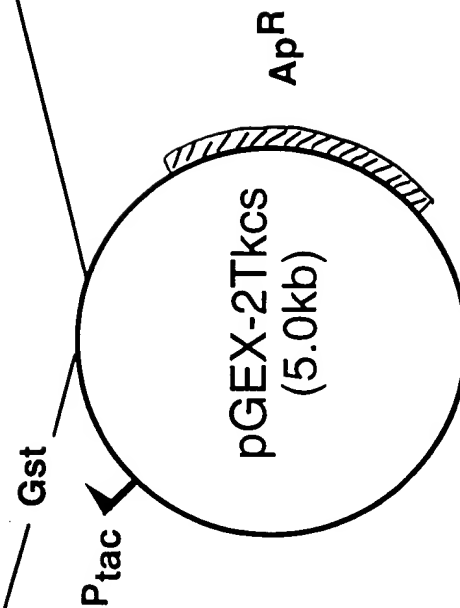AAT TGT TAA CAG ATC CGT CGA CGA GCT CGC TA (530)

Construction of pGst-lox:

A

Linker: C ATG GCT ATA ACT TCG TAT AGC ATA CAT TAT ACG AAG TTA TG
                  CGA TAT TGA AGC ATA TCG TAT GTA ATA TGC TTC AAT AC CTAG
        NcoI   BamHI

B
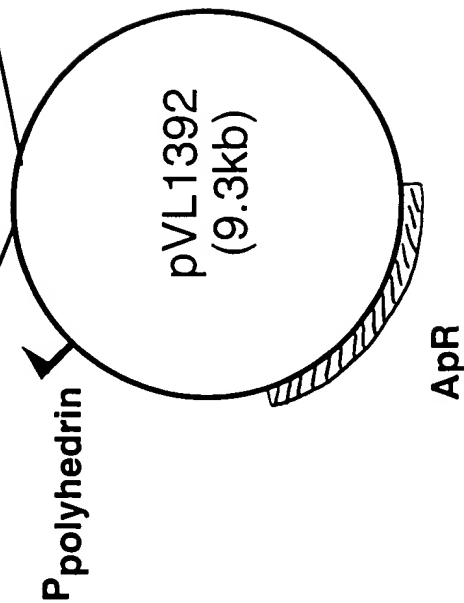
MCS: CAT ATG CCC ATG GCT CGA GGA TCC GAA TTC
     NdeI   NcoI   XhoI   BamHI   EcoRI

Gst

P_tac

pGEX-2Tkcs
(5.0kb)

Ap^R

FIGURE 4

Construction of pVL1392-lox:

A

Linker: GG CCG GAC GTC ATA ACT TCG TAT AGC ATA CAT TAT ACG AAG TTA TG
         C CTG CAG TAT TGA AGC ATA TCG TAT GTA ATA TGC TTC AAT AC CTAG

         NotI   BamHI

B

MCS: BglII / PstI / **NotI** / XmaI / EcoRI / XbaI / SmaI / **BamHI**

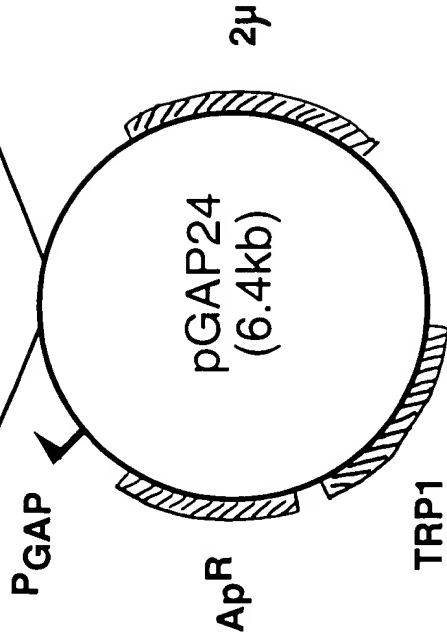P polyhedrin

pVL1392
(9.3kb)

ApR

FIGURE 5

Construction of pGAP24-lox:

A

Linker: T,CGA GAC GTC ATA ACT TCG TAT AGC ATA CAT TAT ACG AAG TTA TGC
         CTG CAG TAT TGA AGC ATA TCG TAT GTA ATA TGC TTC AAT ACG CCGG
         XhoI   NotI

B

MCS: XhoI/BclI/**NotI**/EagI/StyI/AflII

pGAP24 (6.4kb)

P_GAP   2µ   TRP1   Ap^R

FIGURE 6

Construction of pGAL14-lox:

A

Linker: T CGA GAC GTC ATA ACT TCG TAT AGC ATA CAT TAT ACG AAG TTA TGC
         CTG CAG TAT TGA AGC ATA TCG TAT GTA ATA TGC TTC AAT ACG CCGG
         XhoI   NotI
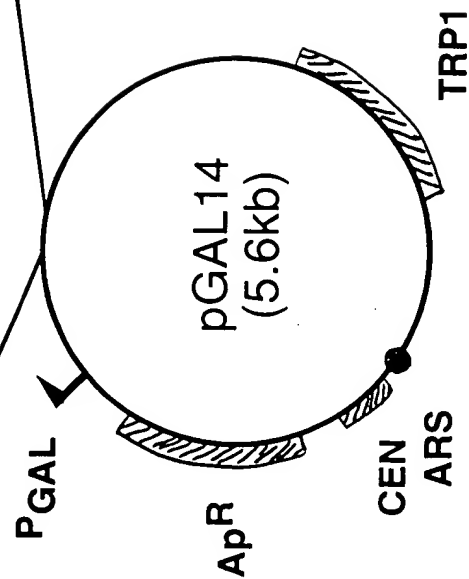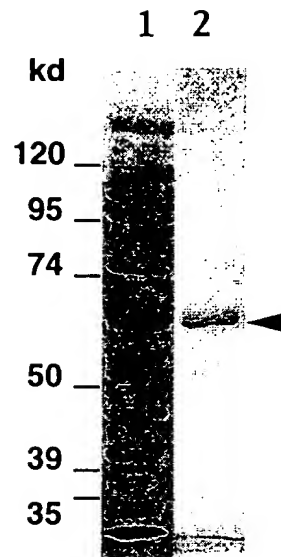
B

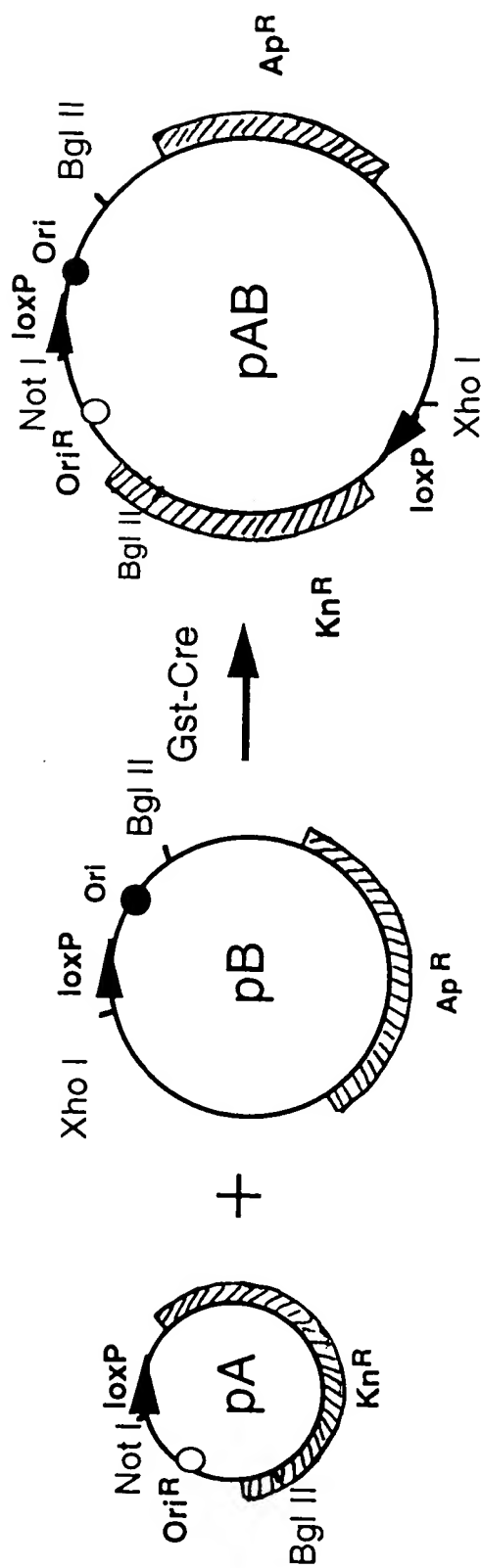MCS: **Sal**I/ClaI/PstI/SmaI/XmaI/SpeI/**Not**I/EagI/SacII/SacI

pGAL14
(5.6kb)

P$_{GAL}$

Ap^R

CEN
ARS

TRP1

FIGURE 7

FIGURE 8

FIGURE 9

A

B

FIGURE 10

A

Gst-Skp1

	M	C		1		2		3	
IPTG:		−	+	−	+	−	+	−	+

kd: 120
95
74
50

B

Gst-Skp1

	C		1		2		3	
IPTG :	−	+	−	+	−	+	−	+

FIGURE 11

C   QLB4

IPTG: -   -   +
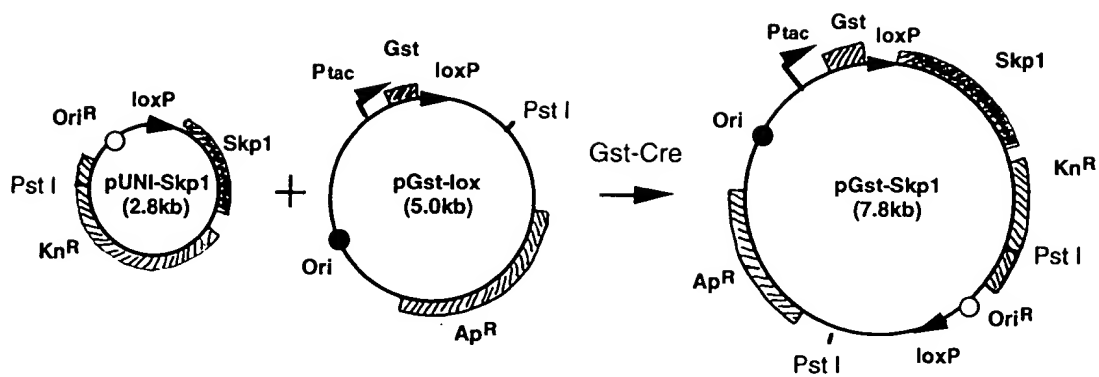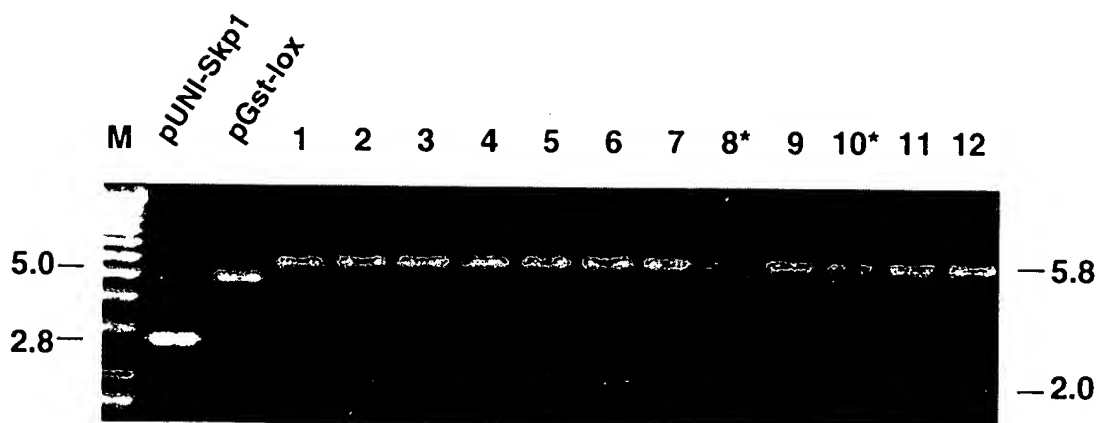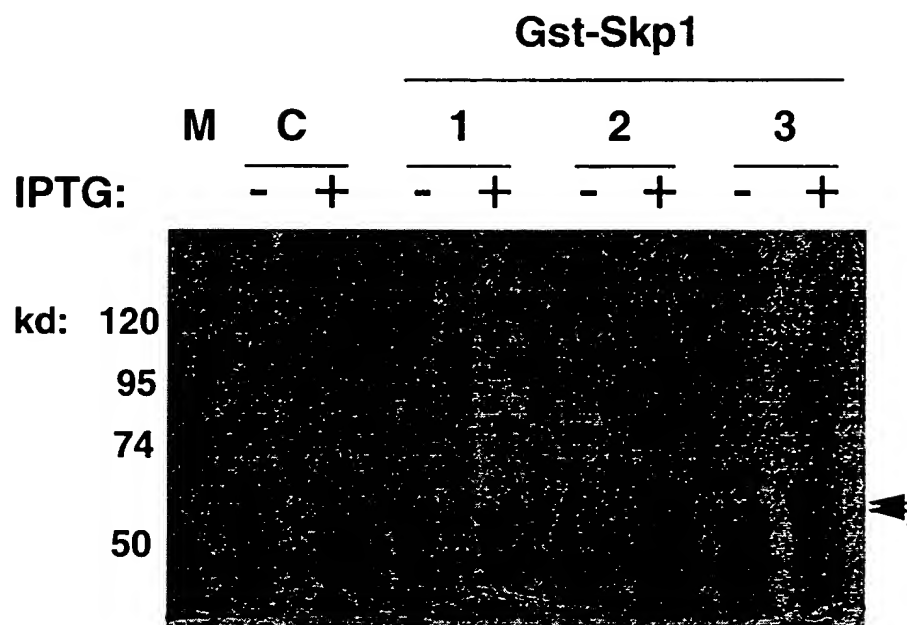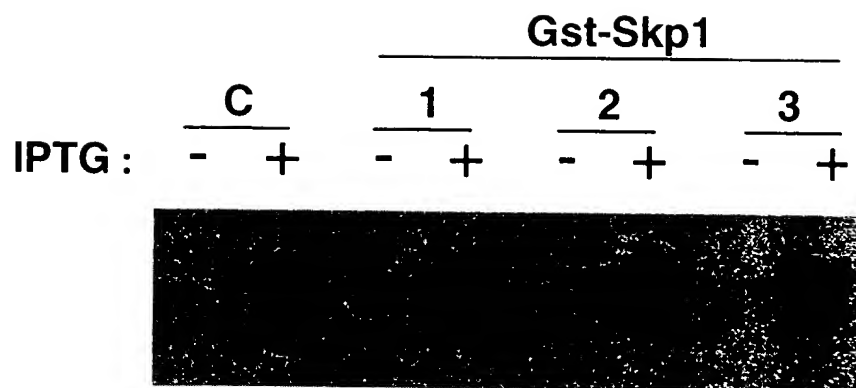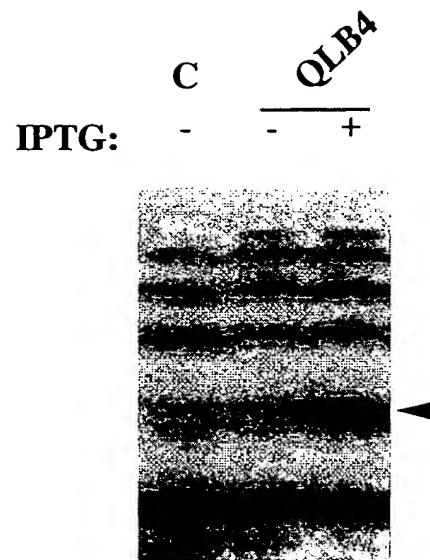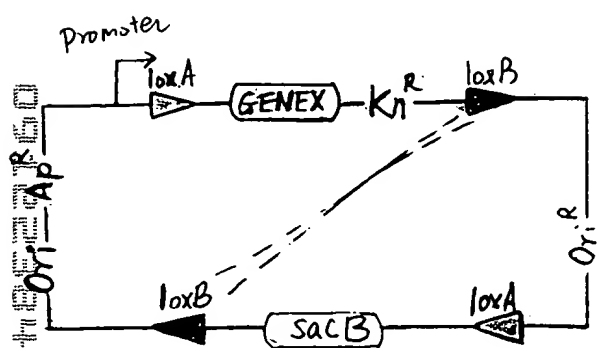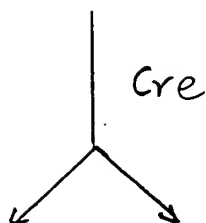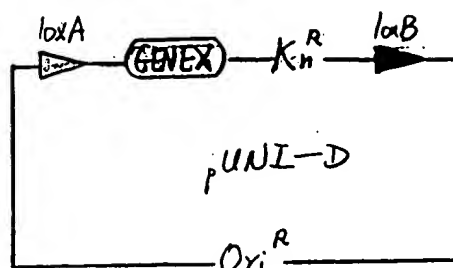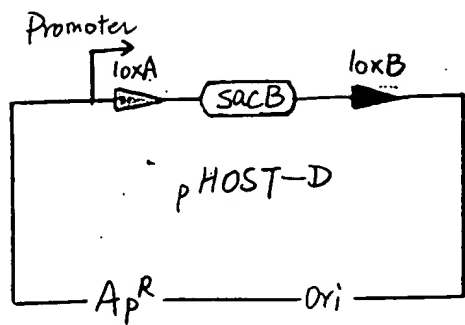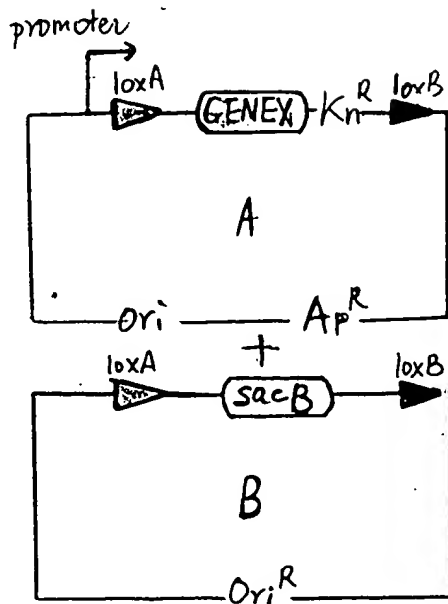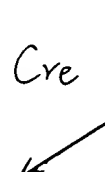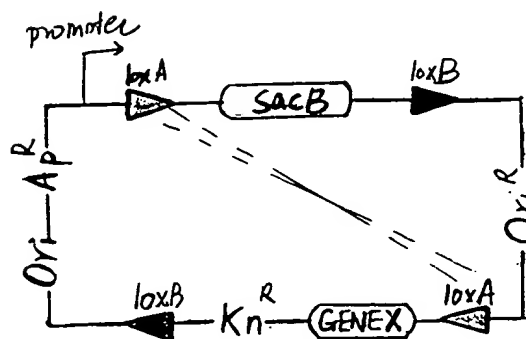
FIGURE 12

FIGURE 13

loxP: ATAACTTCGTATA GCATACAT TATACGAAGTTAT
1 2 3 4 5 6 7 8 9 10 11 12 13   13 12 11 10 9 8 7 6 5 4 3 2 1

        T   C
       | |
loxP2: ATAACTTCGTATA GCATACAT TATACGAAGTTAT
1 2 3 4 5 6 7 8 9 10 11 12 13   13 12 11 10 9 8 7 6 5 4 3 2 1

                       T
                       |
loxP3: ATAACTTCGTATA GCATACAT TATACGAAGTTAT
1 2 3 4 5 6 7 8 9 10 11 12 13   13 12 11 10 9 8 7 6 5 4 3 2 1

       T   C   T
       | | |
loxP23 ATAACTTCGTATA GCATACAT TATACGAAGTTAT
1 2 3 4 5 6 7 8 9 10 11 12 13   13 12 11 10 9 8 7 6 5 4 3 2 1
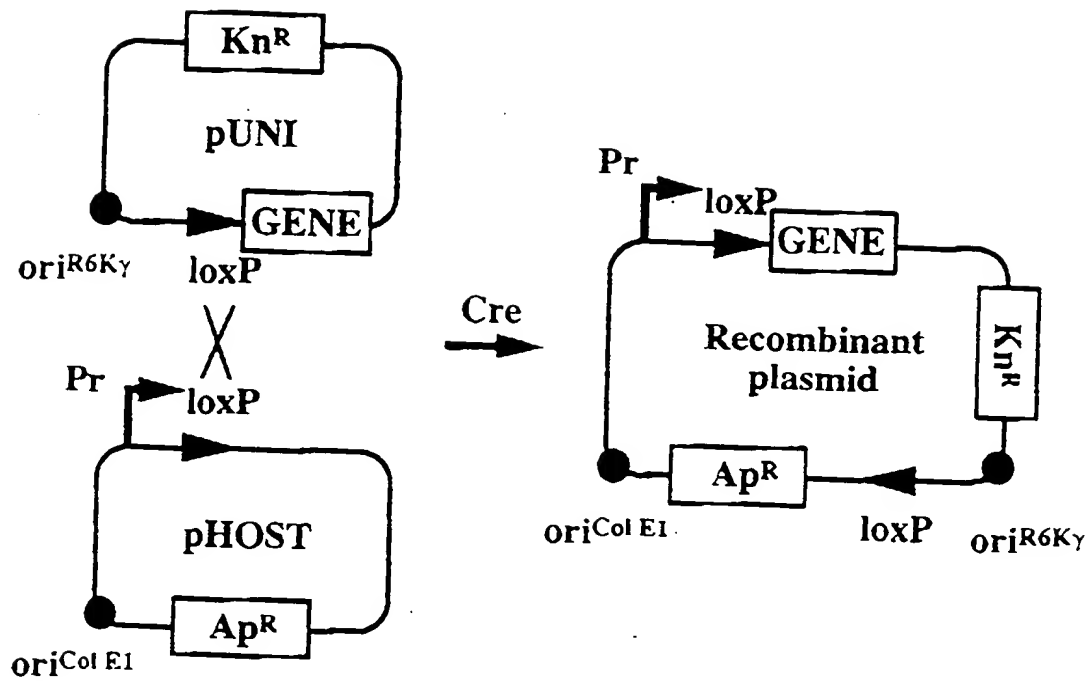
FIGURE 14

FIGURE 15

GST-Cre (μg)	number of Ap^R transformants	number of Kn^R transformants	Kn^R/Ap^R (%)
0	4.0×10^5	0	0
0.02	3.0×10^5	231	0.1
0.04	2.3×10^5	406	0.2
0.06	2.4×10^5	868	0.4
0.08	3.3×10^5	1,336	0.4
0.10	6.0×10^4	594	1.0
0.20	7.8×10^4	580	0.7
0.40	5.8×10^4	1,910	3.3
0.60	9.2×10^4	10,750	11.7
0.80	3.1×10^5	28,660	9.2
1.00	1.0×10^5	16,840	16.8
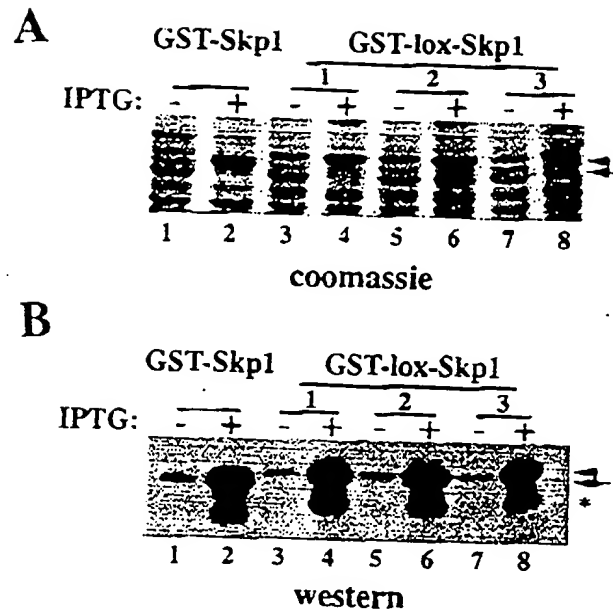
FIGURE 16

A GST-Skp1   GST-lox-Skp1

IPTG: - + - + - + - +

1 2 3 4 5 6 7 8

coomassie

B GST-Skp1   GST-lox-Skp1

IPTG: - + - + - + - +

1 2 3 4 5 6 7 8

western

FIGURE 17

Control   Myc3-Rar4   Control   Myc3-lox-Rad53

loxP loxH

1   2   3   4   5   6

yeast

FIGURE 18

insect cell

FIGURE 19

Control HA3-lox-F3

1   2
mammalian
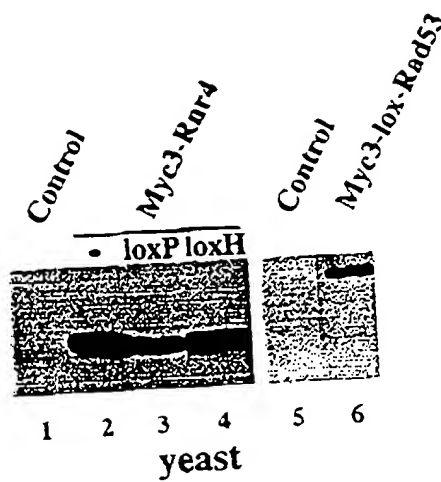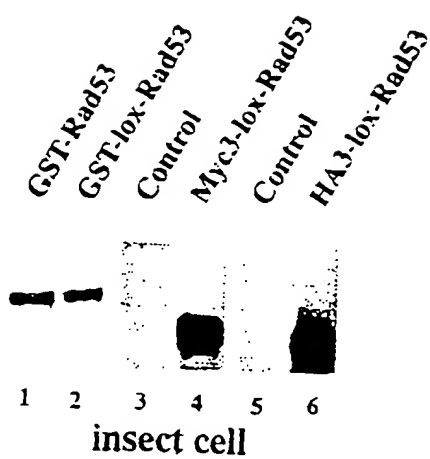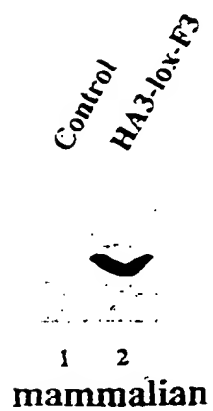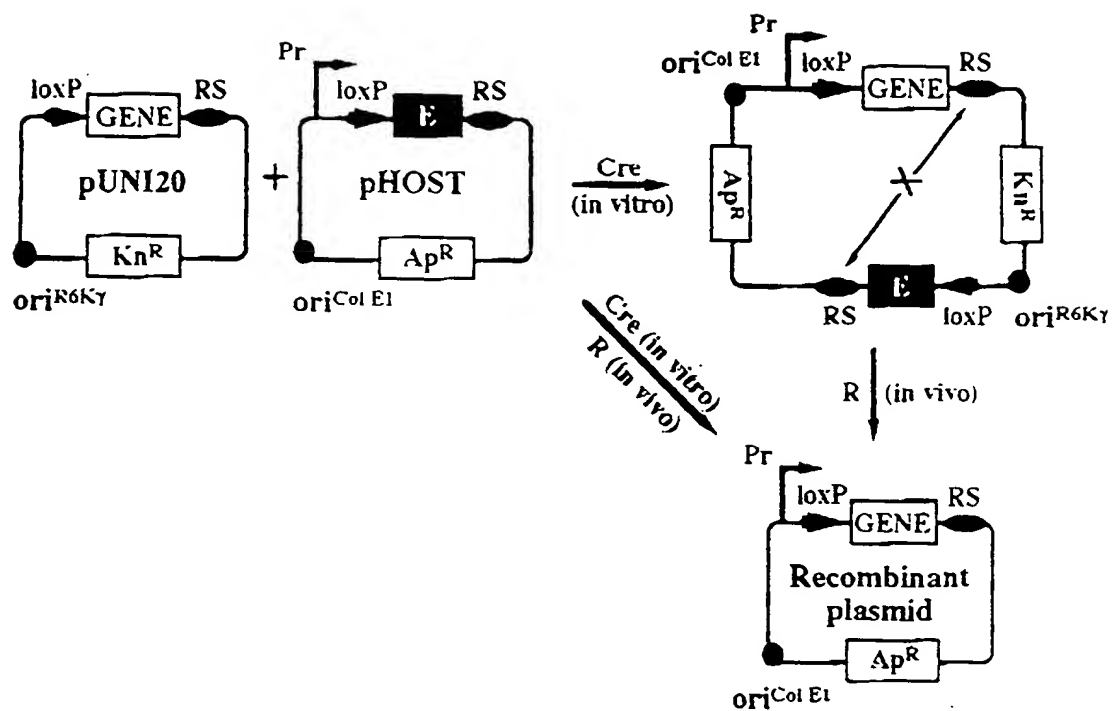
FIGURE 20

FIGURE 21

Pvu II restriction analysis of recombinant
plasmids made by one-step POT

FIGURE 22

Vector

Vector + Insert
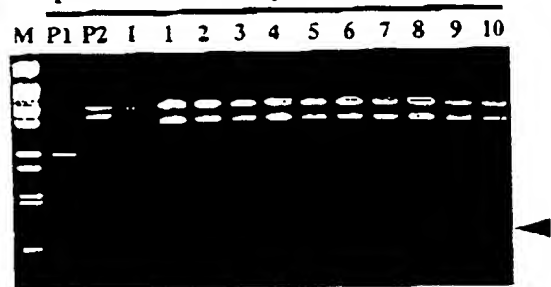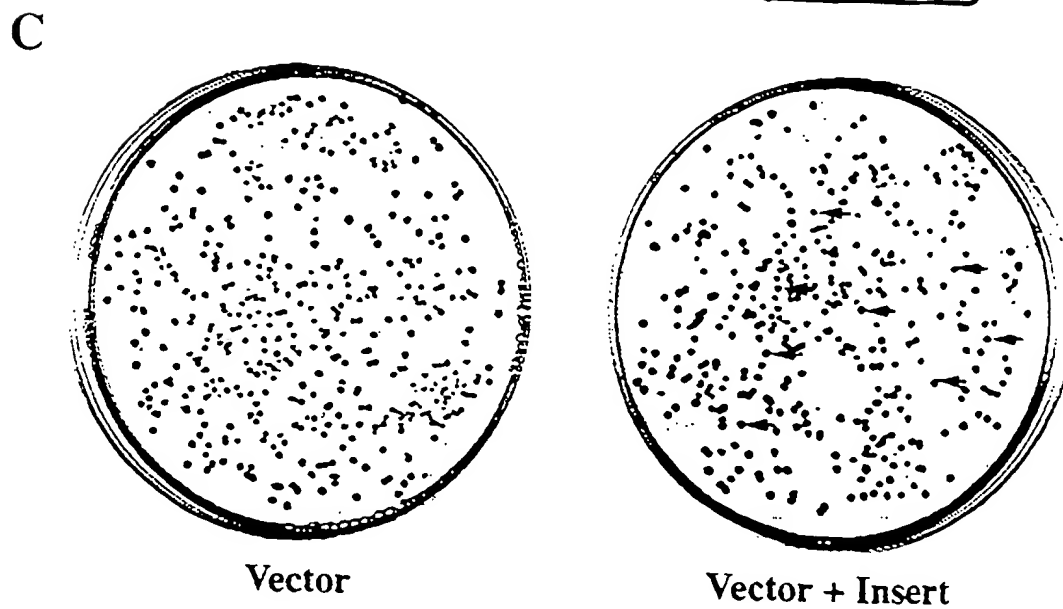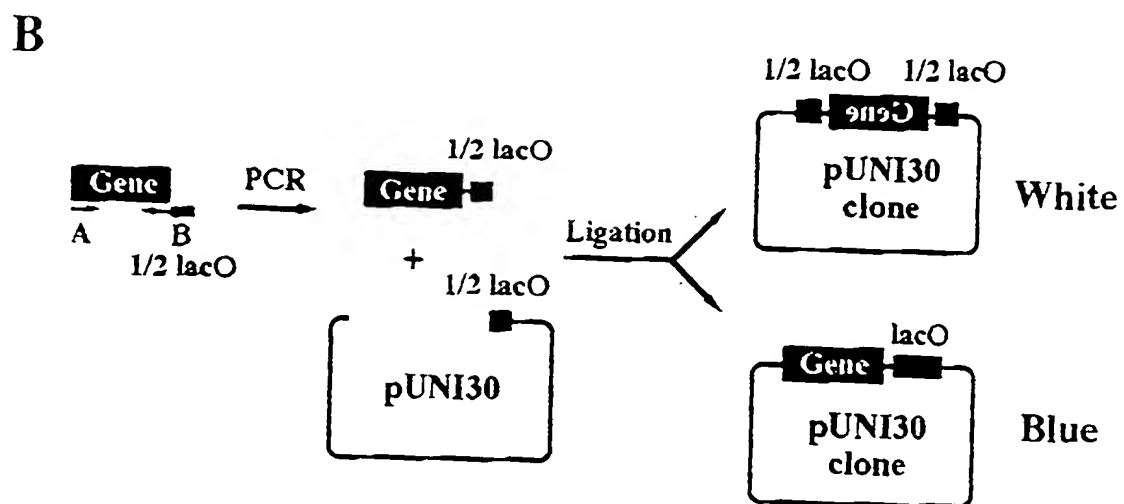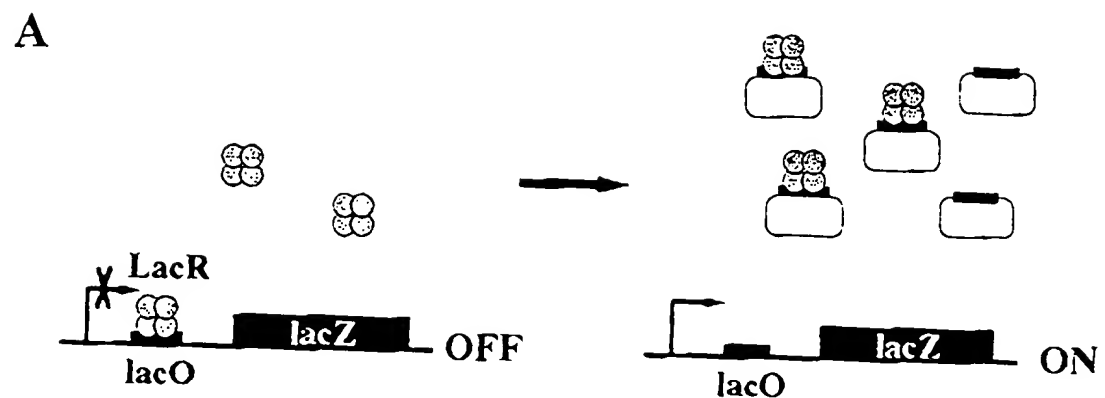
FIGURE 23
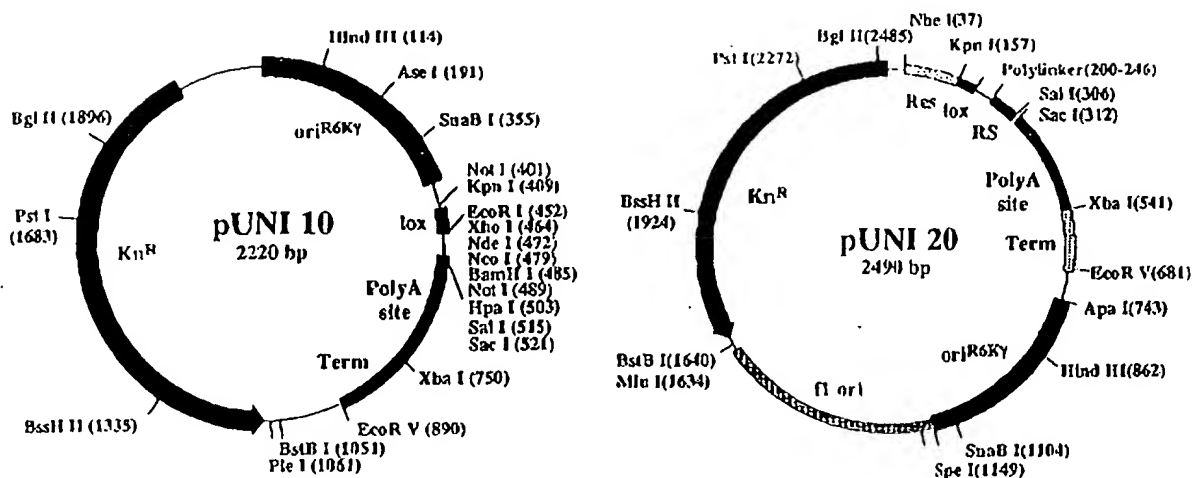
pUNI 10 Polylinker Sequence

```
(401) Not I    Kpn I                LOX
GC GGC CGC GGT ACC ATA ACT TCG TAT AGC ATA CAT TAT ACG A

          EcoR I    Sma I    Xho I       Nde I     Nco I
AG TTA TCT GGA ATT CCC CGG GCT CGA GAA CAT ATG GCC ATG G

  BamHI      Not I          Hpa I          Sal I    Sac I (530)
GG ATC CGC GGC CGC AAT TGT TAA CAG ATC CGT CGA CGA GCT
```

pUNI 20 Polylinker Sequence

```
(157) Kpnl                          LOX
GGT ACC ATA ACT TCG TAT AGC ATA CAT TAT ACG AAG TTA T

    EcoR I    Sma I    Xho I      Nde I     Nco I    BamHI
CT GGA ATT CCC CGG GCT CGA GAACAT ATG GCC ATG GGG ATC

  Not 1  (246)
CGC GGC CGC
```
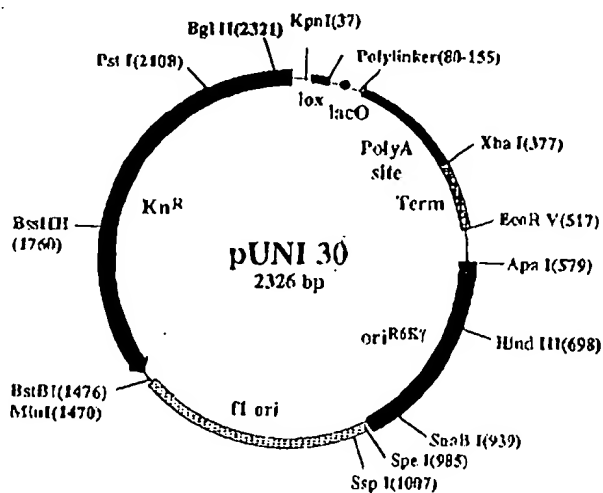
pUNI 30 Polylinker Sequence

```
(37) Kpnl                           LOX
GGT ACC ATA ACT TCG TAT AGC ATA CAT TAT ACG AAG TTA TC

    EcoR I    Sma I    Xho I                Eco47III
T GGA ATT CCC CGG GCT CGA GCC AGT CCA GCG CTC ACA ATT
                                          half lacO

     Not I        Hpa I            Sal I    Sac I  (155)
GCG GCC GCA ATT GTT AAC AGA TCC GTC GAC GAG CTC GC
              MunI
```
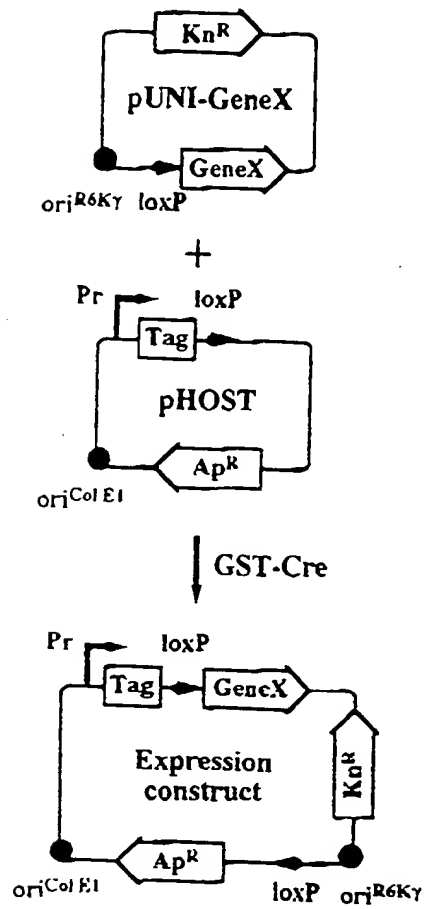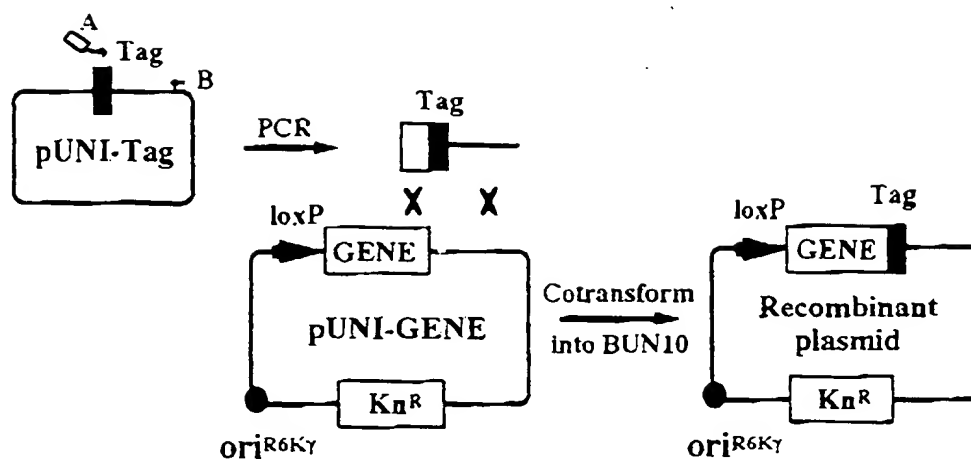
FIGURE 24

FIGURE 25

FIGURE 26A

SEQUENCE DESCRIPTION: SEQ ID NO:1:

```
AATTCTGTCA GCCGTTAAGT GTTCCTGTGT CACTGAAAAT TGCTTTGAGA GGCTCTAAGG
60

GCTTCTCAGT GCGTTACATC CCTGGCTTGT TGTCCACAAC CGTTAAACCT TAAAAGCTTT
120

AAAAGCCTTA TATATTCTTT TTTTTCTTAT AAAACTTAAA ACCTTAGAGG CTATTTAAGT
180

TGCTGATTTA TATTAATTTT ATTGTTCAAA CATGAGAGCT TAGTACGTGA AACATGAGAG
240

CTTAGTACGT TAGCCATGAG AGCTTAGTAC GTTAGCCATG AGGGTTTAGT TCGTTAAACA
300

TGAGAGCTTA GTACGTTAAA CATGAGAGCT TAGTACGTGA AACATGAGAG CTTAGTACGT
360

ACTATCAACA GGTTGAACTG CTGATCAACA GATCCTCTAC GCGGCCGCGG TACCATAACT
420

TCGTATAGCA TACATTATAC GAAGTTATCT GGAATTCCCC GGGCTCGAGA ACATATGGCC
480

ATGGGGATCC GCGGCCGCAA TTGTTAACAG ATCCGTCGAC GAGCTCGCTA TCAGCCTCGA
540

CTGTGCCTTC TAGTTGCCAG CCATCTGTTG TTTGCCCCTC CCCCGTGCCT TCCTTGACCC
600

TGGAAGGTGC CACTCCCACT GTCCTTTCCT AATAAAATGA GGAAATTGCA TCGCATTGTC
660

TGAGTAGGTG TCATTCTATT CTGGGGGGTG GGGTGGGGCA GGACAGCAAG GGGGAGGATT
720

GGGAAGACAA TAGCAGGCAT GCTGGGGATT CTAGAAGATC CGGCTGCTAA CAAAGCCCGA
780

AAGGAAGCTG AGTTGGCTGC TGCCACCGCT GAGCAATAAC TAGCATAACC CCTTGGGGCC
840

TCTAAACGGG TCTTGAGGGG TTTTTTGCTG AAAGGAGGAA CTATATCCGG ATATCCCGGG
900

GTGGGCGAAG AACTCCAGCA TGAGATCCCC GCGCTGGAGG ATCATCCAGC CGGCGTCCCG
960

GAAAACGATT CCGAAGCCCA ACCTTTCATA GAAGGCGGCG GTGGAATCGA AATCTCGTGA
1020

TGGCAGGTTG GGCGTCGCTT GGTCGGTCAT TTCGAACCCC AGAGTCCCGC TCAGAAGAAC
1080
```

TCGTCAAGAA GGCGATAGAA GGCGATGCGC TGCGAATCGG GAGCGGCGAT ACCGTAAAGC
1140

ACGAGGAAGC GGTCAGCCCA TTCGCCGCCA AGCTCTTCAG CAATATCACG GGTAGCCAAC
1200

GCTATGTCCT GATAGCGGTC CGCCACACCC AGCCGGCCAC AGTCGATGAA TCCAGAAAAG
1260

CGGCCATTTT CCACCATGAT ATTCGGCAAG CAGGCATCGC CATGGGTCAC GACGAGATCC
1320

TCGCCGTCGG GCATGCGCGC CTTGAGCCTG GCGAACAGTT CGGCTGGCGC GAGCCCCTGA
1380

TGCTCTTCGT CCAGATCATC CTGATCGACA AGACCGGCTT CCATCCGAGT ACGTGCTCGC
1440

TCGATGCGAT GTTTCGCTTG GTGGTCGAAT GGGCAGGTAG CCGGATCAAG CGTATGCAGC
1500

CGCCGCATTG CATCAGCCAT GATGGATACT TTCTCGGCAG GAGCAAGGTG AGATGACAGG
1560

AGATCCTGCC CCGGCACTTC GCCCAATAGC AGCCAGTCCC TTCCCGCTTC AGTGACAACG
1620

TCGAGCACAG CTGCGCAAGG AACGCCCGTC GTGGCCAGCC ACGATAGCCG CGCTGCCTCG
1680

TCCTGCAGTT CATTCAGGGC ACCGGACAGG TCGGTCTTGA CAAAAAGAAC CGGGCGCCCC
1740

TGCGCTGACA GCCGGAACAC GGCGGCATCA GAGCAGCCGA TTGTCTGTTG TGCCCAGTCA
1800

TAGCCGAATA GCCTCTCCAC CCAAGCGGCC GGAGAACCTG CGTGCAATCC ATCTTGTTCA
1860

ATCATGCGAA ACGATCCTCA TCCTGTCTCT TGATCAGATC TTGATCCCCT GCGCCATCAG
1920

ATCCTTGGCG GCAAGAAAGC CATCCAGTTT ACTTTGCAGG GCTTCCCAAC CTTACCAGAG
1980

GGCGCCCCAG CTGGCAATTC CGGTTCGCTT GCTGTCCATA AAACCGCCCA GTCTAGCTAT
2040

CGCCATGTAA GCCCACTGCA AGCTACCTGC TTTCTCTTTG CGCTTGCGTT TTCCCTTGTC
2100

CAGATAGCCC AGTAGCTGAC ATTCATCCGG GGTCAGCACC GTTTCTGCGG ACTGGCTTTC
2160

TACGTGTTCC GCTTCCTTTA GCAGCCCTTG CGCCCTGAGT GCTTGCGGCA GCGTGAAGCT
2220

FIGURE 26B

SEQUENCE DESCRIPTION: SEQ ID NO:10:

```
ATG TCC CCT ATA CTA GGT TAT TGG AAA ATT AAG GGC CTT GTG CAA CCC
48
Met Ser Pro Ile Leu Gly Tyr Trp Lys Ile Lys Gly Leu Val Gln Pro
 1               5              10              15

ACT CGA CTT CTT TTG GAA TAT CTT GAA GAA AAA TAT GAA GAG CAT TTG
96
Thr Arg Leu Leu Leu Glu Tyr Leu Glu Glu Lys Tyr Glu Glu His Leu
             20              25              30

TAT GAG CGC GAT GAA GGT GAT AAA TGG CGA AAC AAA AAG TTT GAA TTG
144
Tyr Glu Arg Asp Glu Gly Asp Lys Trp Arg Asn Lys Lys Phe Glu Leu
         35              40              45

GGT TTG GAG TTT CCC AAT CTT CCT TAT TAT ATT GAT GGT GAT GTT AAA
192
Gly Leu Glu Phe Pro Asn Leu Pro Tyr Tyr Ile Asp Gly Asp Val Lys
     50              55              60

TTA ACA CAG TCT ATG GCC ATC ATA CGT TAT ATA GCT GAC AAG CAC AAC
240
Leu Thr Gln Ser Met Ala Ile Ile Arg Tyr Ile Ala Asp Lys His Asn
 65              70              75              80

ATG TTG GGT GGT TGT CCA AAA GAG CGT GCA GAG ATT TCA ATG CTT GAA
288
Met Leu Gly Gly Cys Pro Lys Glu Arg Ala Glu Ile Ser Met Leu Glu
             85              90              95

GGA GCG GTT TTG GAT ATT AGA TAC GGT GTT TCG AGA ATT GCA TAT AGT
336
Gly Ala Val Leu Asp Ile Arg Tyr Gly Val Ser Arg Ile Ala Tyr Ser
             100             105             110

AAA GAC TTT GAA ACT CTC AAA GTT GAT TTT CTT AGC AAG CTA CCT GAA
384
Lys Asp Phe Glu Thr Leu Lys Val Asp Phe Leu Ser Lys Leu Pro Glu
         115             120             125

ATG CTG AAA ATG TTC GAA GAT CGT TTA TGT CAT AAA ACA TAT TTA AAT
432
Met Leu Lys Met Phe Glu Asp Arg Leu Cys His Lys Thr Tyr Leu Asn
         130             135             140

GGT GAT CAT GTA ACC CAT CCT GAC TTC ATG TTG TAT GAC GCT CTT GAT
480
Gly Asp His Val Thr His Pro Asp Phe Met Leu Tyr Asp Ala Leu Asp
145             150             155             160
```

GTT GTT TTA TAC ATG GAC CCA ATG TGC CTG GAT GCG TTC CCA AAA TTA
528
Val Val Leu Tyr Met Asp Pro Met Cys Leu Asp Ala Phe Pro Lys Leu
165   170   175

GTT TGT TTT AAA AAA CGT ATT GAA GCT ATC CCA CAA ATT GAT AAG TAC
576
Val Cys Phe Lys Lys Arg Ile Glu Ala Ile Pro Gln Ile Asp Lys Tyr
180   185   190

TTG AAA TCC AGC AAG TAT ATA GCA TGG CCT TTG CAG GGC TGG CAA GCC
624
Leu Lys Ser Ser Lys Tyr Ile Ala Trp Pro Leu Gln Gly Trp Gln Ala
195   200   205

ACG TTT GGT GGT GGC GAC CAT CCT CCA AAA TCG GAT CTG GTT CCG CGT
672
Thr Phe Gly Gly Gly Asp His Pro Pro Lys Ser Asp Leu Val Pro Arg
210   215   220

GGA TCT CGT CGT GCA TCT GTT GGA TCG CAT ATG CCC ATG GCC AAT TTA
720
Gly Ser Arg Arg Ala Ser Val Gly Ser His Met Pro Met Ala Asn Leu
225   230   235   240

CTG ACC GTA CAC CAA AAT TTG CCT GCA TTA CCG GTC GAT GCA ACG AGT
768
Leu Thr Val His Gln Asn Leu Pro Ala Leu Pro Val Asp Ala Thr Ser
245   250   255

GAT GAG GTT CGC AAG AAC CTG ATG GAC ATG TTC AGG GAT CGC CAG GCG
816
Asp Glu Val Arg Lys Asn Leu Met Asp Met Phe Arg Asp Arg Gln Ala
260   265   270

TTT TCT GAG CAT ACC TGG AAA ATG CTT CTG TCC GTT TGC CGG TCG TGG
864
Phe Ser Glu His Thr Trp Lys Met Leu Leu Ser Val Cys Arg Ser Trp
275   280   285

GCG GCA TGG TGC AAG TTG AAT AAC CGG AAA TGG TTT CCC GCA GAA CCT
912
Ala Ala Trp Cys Lys Leu Asn Asn Arg Lys Trp Phe Pro Ala Glu Pro
290   295   300

GAA GAT GTT CGC GAT TAT CTT CTA TAT CTT CAG GCG CGC GGT CTG GCA
960
Glu Asp Val Arg Asp Tyr Leu Leu Tyr Leu Gln Ala Arg Gly Leu Ala
305   310   315   320

GTA AAA ACT ATC CAG CAA CAT TTG GGC CAG CTA AAC ATG CTT CAT CGT
1008
Val Lys Thr Ile Gln Gln His Leu Gly Gln Leu Asn Met Leu His Arg
325   330   335

CGG TCC GGG CTG CCA CGA CCA AGT GAC AGC AAT GCT GTT TCA CTG GTT
1056
Arg Ser Gly Leu Pro Arg Pro Ser Asp Ser Asn Ala Val Ser Leu Val
340   345   350

```
ATG CGG CGG ATC CGA AAA GAA AAC GTT GAT GCC GGT GAA CGT GCA AAA
1104
Met Arg Arg Ile Arg Lys Glu Asn Val Asp Ala Gly Glu Arg Ala Lys
        355             360             365

CAG GCT CTA GCG TTC GAA CGC ACT GAT TTC GAC CAG GTT CGT TCA CTC
1152
Gln Ala Leu Ala Phe Glu Arg Thr Asp Phe Asp Gln Val Arg Ser Leu
        370             375             380

ATG GAA AAT AGC GAT CGC TGC CAG GAT ATA CGT AAT CTG GCA TTT CTG
1200
Met Glu Asn Ser Asp Arg Cys Gln Asp Ile Arg Asn Leu Ala Phe Leu
385             390             395             400

GGG ATT GCT TAT AAC ACC CTG TTA CGT ATA GCC GAA ATT GCC AGG ATC
1248
Gly Ile Ala Tyr Asn Thr Leu Leu Arg Ile Ala Glu Ile Ala Arg Ile
            405             410             415

AGG GTT AAA GAT ATC TCA CGT ACT GAC GGT GGG AGA ATG TTA ATC CAT
1296
Arg Val Lys Asp Ile Ser Arg Thr Asp Gly Gly Arg Met Leu Ile His
            420             425             430

ATT GGC AGA ACG AAA ACG CTG GTT AGC ACC GCA GGT GTA GAG AAG GCA
1344
Ile Gly Arg Thr Lys Thr Leu Val Ser Thr Ala Gly Val Glu Lys Ala
        435             440             445

CTT AGC CTG GGG GTA ACT AAA CTG GTC GAG CGA TGG ATT TCC GTC TCT
1392
Leu Ser Leu Gly Val Thr Lys Leu Val Glu Arg Trp Ile Ser Val Ser
        450             455             460

GGT GTA GCT GAT GAT CCG AAT AAC TAC CTG TTT TGC CGG GTC AGA AAA
1440
Gly Val Ala Asp Asp Pro Asn Asn Tyr Leu Phe Cys Arg Val Arg Lys
465             470             475             480

AAT GGT GTT GCC GCG CCA TCT GCC ACC AGC CAG CTA TCA ACT CGC GCC
1488
Asn Gly Val Ala Ala Pro Ser Ala Thr Ser Gln Leu Ser Thr Arg Ala
            485             490             495

CTG GAA GGG ATT TTT GAA GCA ACT CAT CGA TTG ATT TAC GGC GCT AAG
1536
Leu Glu Gly Ile Phe Glu Ala Thr His Arg Leu Ile Tyr Gly Ala Lys
        500             505             510

GAT GAC TCT GGT CAG AGA TAC CTG GCC TGG TCT GGA CAC AGT GCC CGT
1584
Asp Asp Ser Gly Gln Arg Tyr Leu Ala Trp Ser Gly His Ser Ala Arg
        515             520             525

GTC GGA GCC GCG CGA GAT ATG GCC CGC GCT GGA GTT TCA ATA CCG GAG
1632
Val Gly Ala Ala Arg Asp Met Ala Arg Ala Gly Val Ser Ile Pro Glu
        530             535             540
```

```
ATC ATG CAA GCT GGT GGC TGG ACC AAT GTA AAT ATT GTC ATG AAC TAT
1680
Ile Met Gln Ala Gly Gly Trp Thr Asn Val Asn Ile Val Met Asn Tyr
545             550             555             560

ATC CGT AAC CTG GAT AGT GAA ACA GGG GCA ATG GTG CGC CTG CTG GAA
1728
Ile Arg Asn Leu Asp Ser Glu Thr Gly Ala Met Val Arg Leu Leu Glu
            565             570             575

GAT GGC GAT TAG
1740
Asp Gly Asp
```

FIGURE 26C

SEQUENCE DESCRIPTION: SEQ ID NO:11:

```
Met Ser Pro Ile Leu Gly Tyr Trp Lys Ile Lys Gly Leu Val Gln Pro
 1               5               10                  15

Thr Arg Leu Leu Leu Glu Tyr Leu Glu Glu Lys Tyr Glu Glu His Leu
            20              25              30

Tyr Glu Arg Asp Glu Gly Asp Lys Trp Arg Asn Lys Lys Phe Glu Leu
        35              40              45

Gly Leu Glu Phe Pro Asn Leu Pro Tyr Tyr Ile Asp Gly Asp Val Lys
    50               55              60

Leu Thr Gln Ser Met Ala Ile Ile Arg Tyr Ile Ala Asp Lys His Asn
65              70              75                      80

Met Leu Gly Gly Cys Pro Lys Glu Arg Ala Glu Ile Ser Met Leu Glu
            85              90                      95

Gly Ala Val Leu Asp Ile Arg Tyr Gly Val Ser Arg Ile Ala Tyr Ser
        100             105             110

Lys Asp Phe Glu Thr Leu Lys Val Asp Phe Leu Ser Lys Leu Pro Glu
        115             120             125

Met Leu Lys Met Phe Glu Asp Arg Leu Cys His Lys Thr Tyr Leu Asn
    130             135             140

Gly Asp His Val Thr His Pro Asp Phe Met Leu Tyr Asp Ala Leu Asp
145             150             155                     160

Val Val Leu Tyr Met Asp Pro Met Cys Leu Asp Ala Phe Pro Lys Leu
            165             170             175

Val Cys Phe Lys Lys Arg Ile Glu Ala Ile Pro Gln Ile Asp Lys Tyr
        180             185             190

Leu Lys Ser Ser Lys Tyr Ile Ala Trp Pro Leu Gln Gly Trp Gln Ala
        195             200             205

Thr Phe Gly Gly Gly Asp His Pro Pro Lys Ser Asp Leu Val Pro Arg
    210             215             220

Gly Ser Arg Arg Ala Ser Val Gly Ser His Met Pro Met Ala Asn Leu
225             230             235             240

Leu Thr Val His Gln Asn Leu Pro Ala Leu Pro Val Asp Ala Thr Ser
            245             250             255

Asp Glu Val Arg Lys Asn Leu Met Asp Met Phe Arg Asp Arg Gln Ala
        260             265             270

Phe Ser Glu His Thr Trp Lys Met Leu Leu Ser Val Cys Arg Ser Trp
```

```
                275                    280                    285
Ala Ala Trp Cys Lys Leu Asn Asn Arg Lys Trp Phe Pro Ala Glu Pro
    290                 295                 300

Glu Asp Val Arg Asp Tyr Leu Leu Tyr Leu Gln Ala Arg Gly Leu Ala
305                 310                 315                 320

Val Lys Thr Ile Gln Gln His Leu Gly Gln Leu Asn Met Leu His Arg
                325                 330                 335

Arg Ser Gly Leu Pro Arg Pro Ser Asp Ser Asn Ala Val Ser Leu Val
            340                 345                 350

Met Arg Arg Ile Arg Lys Glu Asn Val Asp Ala Gly Glu Arg Ala Lys
        355                 360                 365

Gln Ala Leu Ala Phe Glu Arg Thr Asp Phe Asp Gln Val Arg Ser Leu
    370                 375                 380

Met Glu Asn Ser Asp Arg Cys Gln Asp Ile Arg Asn Leu Ala Phe Leu
385                 390                 395                 400

Gly Ile Ala Tyr Asn Thr Leu Leu Arg Ile Ala Glu Ile Ala Arg Ile
                405                 410                 415

Arg Val Lys Asp Ile Ser Arg Thr Asp Gly Gly Arg Met Leu Ile His
            420                 425                 430

Ile Gly Arg Thr Lys Thr Leu Val Ser Thr Ala Gly Val Glu Lys Ala
        435                 440                 445

Leu Ser Leu Gly Val Thr Lys Leu Val Glu Arg Trp Ile Ser Val Ser
    450                 455                 460

Gly Val Ala Asp Asp Pro Asn Asn Tyr Leu Phe Cys Arg Val Arg Lys
465                 470                 475                 480

Asn Gly Val Ala Ala Pro Ser Ala Thr Ser Gln Leu Ser Thr Arg Ala
                485                 490                 495

Leu Glu Gly Ile Phe Glu Ala Thr His Arg Leu Ile Tyr Gly Ala Lys
            500                 505                 510

Asp Asp Ser Gly Gln Arg Tyr Leu Ala Trp Ser Gly His Ser Ala Arg
            515                 520                 525

Val Gly Ala Ala Arg Asp Met Ala Arg Ala Gly Val Ser Ile Pro Glu
    530                 535                 540

Ile Met Gln Ala Gly Gly Trp Thr Asn Val Asn Ile Val Met Asn Tyr
545                 550                 555                 560

Ile Arg Asn Leu Asp Ser Glu Thr Gly Ala Met Val Arg Leu Leu Glu
                565                 570                 575

Asp Gly Asp
```